Karyopharm Announces Presentation of Selinexor and KPT-9274 Clinical Data at the European Society of Medical Oncology 2017 Annual Meeting

Top-line Phase 1 Selinexor Data in Combination with Chemotherapy Show Encouraging Early Efficacy in Patients with Ovarian and Endometrial Cancers
Top-line Phase 1 KPT-9274 Data Show a Manageable Safety Profile and Early Signals of Anti-Tumor Activity

NEWTON, Mass., Sept. 08, 2017 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced two upcoming poster presentations at the European Society of Medical Oncology (ESMO) 2017 Annual Meeting, taking place September 8-12, 2017 in Madrid, Spain. One poster will describe Phase 1 data from an ongoing investigator-sponsored trial (IST) evaluating the safety and tolerability of the Company's lead product candidate, selinexor (KPT-330), an oral Selective Inhibitor of Nuclear Export / SINE™ compound, in combination with paclitaxel and carboplatin in patients with advanced ovarian or endometrial cancers. The other poster will describe Phase 1 clinical data from an ongoing study evaluating the safety and tolerability of KPT-9274, Karyopharm's oral, dual inhibitor of p21-activated kinase 4 (PAK4) and nicotinamide phosphoribosyltransferase (NAMPT) in patients with advanced solid malignancies or non-Hodgkin's lymphoma (NHL).

"We are encouraged by the manageable safety profile and compelling responses seen in Dr. Makker's Phase 1 study evaluating oral selinexor in combination with standard chemotherapies," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "These findings continue to build upon the growing body of clinical data supporting selinexor's potential in gynecological malignancies and we look forward to seeing future data from the expansion cohorts. For oral KPT-9274, we are pleased to be reporting early preliminary data from patients with a wide variety of advanced solid malignancies, which show a manageable safety profile as well as early signals of efficacy."

Phase 1 Study of Selinexor in Combination with Paclitaxel and Carboplatin in Patients with Advanced Ovarian or Endometrial Cancers

Among the 16 patients (12 with uterine cancer and 4 with ovarian cancer) evaluated for safety as of the data cutoff date of August 25, 2017, the most common Grade 2 adverse events (AEs) were leukopenia (43.8%), hyperglycemia (37.5%), fatigue (37.5%) and anemia (31.3%). The most common Grade ≥3 AEs were anemia (62.5%), neutropenia (68.8%), leukopenia (50.0%), lymphopenia (43.8%) and thrombocytopenia (31.3%). Among the 15 patients evaluable for efficacy, 11 responded for an overall response rate of 73%: 1 patient (6.7%) with a complete response and 10 patients (66.7%) with a partial response. Two patients (13.3%) had stable disease and 2 patients (13.3%) had progressive disease. The time on study ranged from 2 to >14.3 months, with 2 patients still on study as of the data cutoff date.

The recommended Phase 2 dose (RP2D) regimen was established as selinexor 60mg flat dose once weekly in combination with carboplatin AUC5 on Day 1 and paclitaxel 80 mg/m2 on Days 1, 8 and 15 of each 21-day cycle. Expansion cohorts for the RP2D regimen are planned.

Phase 1 Study of KPT-9274 in Patients with Advanced Solid Malignancies (including Sarcoma, Colon and Lung Cancer) or Relapsed NHL Following Standard Therapy(s)

Among the 21 patients evaluated for safety as of July 10, 2017, the most common Grade 2 AEs across dose levels were arthralgia (43%), anemia (24%) and fatigue (24%). The most common drug-related Grade ≥3 AEs across dose levels include anemia (38%) and fatigue (5%). Gastrointestinal-related AEs were infrequent and low grade. Among the 18 patients evaluable for preliminary efficacy, there were 6 (33%) with SD, the longest for 7.3 months. Tumor reductions (shrinkage of ~5%, ~15% and ~22% per RECIST v1.1) were observed in all 3 out of 3 patients with NAPRT deficient tumors. In addition, niacin can be safely administered with KPT-9274 and may improve tolerability, particularly anemia. Dose escalation remains ongoing and further evaluation of effects in NAPRT deficient tumors will be undertaken. These study findings indicate that in patients whose disease has progressed despite most available therapies, KPT-9274 can induce tumor shrinkage and disease stabilization.

Details for the Poster Presentations at ESMO 2017:

Title: A Phase 1 Study of Selinexor (S) in Combination with Paclitaxel (P) and Carboplatin (C) in Patients (pts) with Advanced Ovarian (OC) or Endometrial Cancers (EC)
Presenter: Vicky Makker, Memorial Sloan Kettering Cancer Center, New York, New York, USA
Abstract code: 970P
Session: Poster Display Session
Location: Hall 8

Date and Time: Saturday, September 9, 2017 from 13:15 - 14:15 CET

Title: A First in Human Phase 1 Study of KPT-9274, a First in Class Dual Inhibitor of PAK4 and NAMPT, in Patients with Advanced Solid Malignancies or NHL
Presenter: Aung Naing, MD Anderson Cancer Center, Houston, Texas, USA
Abstract code: 374PD
Session: Poster Discussion Session — Developmental Therapeutics
Location: Alicante Auditorium
Date and Time: Saturday, September 9, 2017 from 16:30 - 18:00 CET

About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound. Selinexor functions by binding with and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. This reinitiates and amplifies their tumor suppressor function and is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 2,100 patients have been treated with selinexor and it is currently being evaluated in several mid- and later-phase clinical trials across multiple cancer indications, including in multiple myeloma in a pivotal, randomized Phase 3 study in combination with Velcade® (bortezomib) and low-dose dexamethasone (BOSTON), in combination with low-dose dexamethasone (STORM) and backbone therapies (STOMP), and in diffuse large B-cell lymphoma (SADAL), and liposarcoma (SEAL), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with one or more approved therapies in a variety of tumor types to further inform the Company's clinical development priorities for selinexor. Additional clinical trial information for selinexor is available at www.clinicaltrials.gov.

About KPT-9274

KPT-9274 is a first-in-class, orally bioavailable, small molecule immunometabolic modulator that works through non-competitive dual inhibition of p21-activated kinase 4 (PAK4) and nicotinamide phosphoribosyltransferase (NAMPT). NAMPT and NAPRT (Nicotinate Phosphoribosyltransferas) are the two main pathways for production of the NAD (nicotinamide dinucleotide). About 15-30% of all solid tumors are deficient in NAPRT, making them reliant on NAMPT for NAD production. Co-inhibition of PAK4 and NAMPT is believed to lead to synergistic anti-tumor effects through suppression of ß-catenin by blocking PAK4, leading to both immune cell activation and inhibition of tumor growth, blockade of DNA repair, cell cycle arrest, and energy depletion through NAMPT inhibition, and ultimately apoptosis. KPT-9274 may therefore have both immune-activating and direct antitumor effects. Tumors deficient in NAPRT may be particularly susceptible to KPT-9274's actions. In contrast, normal cells are less sensitive to inhibition by KPT-9274 due in part to their relative genomic stability and lower metabolic demands.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq:KPTI) is a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport and related targets for the treatment of cancer and other major diseases. Karyopharm's SINE™ compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). In addition to single-agent and combination activity against a variety of human cancers, SINE™ compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. Karyopharm, which was founded by Dr. Sharon Shacham, currently has several investigational programs in clinical or preclinical development. For more information, please visit www.karyopharm.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from the Company's current expectations. For example, there can be no guarantee that any of Karyopharm's SINE™ compounds, including selinexor (KPT-330) and KPT-9274, will successfully complete necessary preclinical and clinical development phases or that development of any of Karyopharm's drug candidates will continue. Further, there can be no guarantee that any positive developments in Karyopharm's drug candidate portfolio will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for diseases in which Karyopharm is currently developing its drug candidates; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, which was filed with the Securities and Exchange Commission (SEC) on August 8, 2017, and in

other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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